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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/758,902	01/11/2001	Roberts S. David	PC9047D	1327

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PFIZER INC
150 EAST 42ND STREET
5TH FLOOR - STOP 49
NEW YORK, NY 10017-5612

EXAMINER	
SHAHNAN SHAH, KHATOL S	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 08/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/758,902	DAVID ET AL.	
	Examiner	Art Unit	
	Khatol S Shahnan-Shah	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/24/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' amendment and response received 4/29/2004 is acknowledged. The amendment has been entered. New claim 20 has been added.

2. Currently claims 18-20 are pending and under consideration.

3. Applicants' information disclosure received 5/24/2004 is acknowledged. The references have been considered by the examiner.

Prior Citations of Title 35 Sections

4. The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior office action.

Prior Citations of References

5. The references cited or used as prior art in support of one or more rejections in the instant office action have been previously cited and made of record. No form PTO-892 has been submitted with this office action.

Rejections Withdrawn

6. Rejection of claim 18 under 35 U.S.C. 112 first paragraph, made in paragraph 7 of the office action mailed 1/15/2004 is withdrawn in view of applicants' arguments.

Rejections Maintained

7. Rejection of claims 18-19 under 35 U.S.C. 103, made in paragraph 5 of the office action mailed 12/14/2001, paper # 4 is maintained.

The rejection was as following:

Claims 18-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Green et al. (The veterinary record, May 2, 1987) and Geresi et al. (Ann. Immuno. Hung Vol. 25, pp. 37-40 1985) in view of Wu et al. (The Journal of Immunology, Vol. 148, pp. 1519-1525, 1992) and Gluck et al. (US Patent 5,879,685).

Claims are drawn to a multicomponent clostridial vaccine composition comprising a viral antigen and a saponin adjuvant.

Green et al. teach the formulation of a multivalent clostridial vaccine in analogous art (see page 435) for the purpose of stimulating a protective immune response against multiple strains and species of this pathogen. Green et al. teach multicomponent clostridial vaccines such as Covexin 8, Hepatavac and Tasvax (see table 1). Green et al. teach the inclusion of six or more clostridial immunogens such as toxoids from *Cl. chauvoei, Cl. septicum, Cl. tetani, Cl. nvoyi, Cl. haemalyticum and Cl. perfringins* (type B, C and D) for the realized reduced threat of loss of livestock, wherein the use of six or more of clostridial immunogens would have provided for a broader range of immune response against clostridial pathogens and increase the likelihood of protection against infection by a broader range of species or strains of clostridium. Green et al. teach aluminum hydroxide as the adjuvant (page 438, column 1). Green et al. do not teach viral antigen.

Geresi et al. teach the formulation of multivalent clostridial vaccine compositions, which also comprise a viral immunogen (see page 38). The reference differs from the instantly claimed invention by failing to show the use of saponin as an adjuvant.

Wu et al. show the use of saponin adjuvant in association with an antigen, wherein the exemplified vaccine comprised a viral antigen (see abstract and results in page 1521 and

discussion in page 1523). Wu et al. teach that vaccine formulations containing the saponin adjuvant produced significantly higher titers of antibody than alum absorbed vaccines. Wu et al. do not teach a respiratory virus.

Gluck et al. teach an immunostimulating combination of influenza virus and *Clostridium tetani* (see abstract and claims 6-9).

Therefore, it would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to modify or combine the compositions of Green et al. and Geresi et al., include a respiratory virus taught by Gluck et al. and to include the saponin adjuvant of Wu et al. because all of the references are directed to the formulation of vaccines for the attainment of enhance immune response. One with ordinary skill in art would have been motivated to combine these compositions because Green et al and Geresi et al. both teach the formulation of multicomponent clostridial vaccines, Gluck et al. and Geresi et al. teach the inclusion of viral antigens in bacterial vaccine composition and Wu et al. teach the use of saponin as an adjuvant which provides for an enhanced immune response when in association with a viral antigen. In the absence of evident to the contrary, Green et al. and Geresi et al., in view of Gluck et al. and Wu et al. obviate the instantly claimed invention.

Applicants' arguments filed 4/29/04 have been fully considered but they are not persuasive.

Applicants argue that cited art does not provide any suggestion or motivation to make the claimed invention. Applicants further argue, " that prior to the present invention, there was no recognition in the art that a water-soluble adjuvant such saponin could be used as an adjuvant to enhance immunogenicity of a clostridial antigen". Applicants further argue that the results achieved with the presently claimed vaccine composition are unexpected. In particular, those

skilled in the art would not have reasonably expected that the use of soluble adjuvants that readily dispersed from the injection site and have no depot effect, such as saponin, would be successful in enhancing the potency of the clostridial antigens.

In response to applicants' argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the motivation of combining immunogenic compositions containing *Clostridium* species and respiratory virus is coming from teachings of Gluck et al. Gluck et al. teach an immunostimulating combination of influenza virus and *Clostridium tetani* (see abstract and claims 6-9). Use of different adjuvants such as saponin is well known in the art of vaccine preparation and saponin adjuvant has been commercially available (i.e Quil A) (see Wu et al. page 1519 right column). Therefore one of ordinary skill in the art would have been motivated to replace the aluminum hydroxide adjuvant of Green et al. with the saponin adjuvant.

In response to the applicants' arguments that unexpected results were obtained when the depot alum adjuvant was replaced by the soluble adjuvants that are readily dispersed from the injection site and has no depot effect such as saponin. The examiner brings applicant' attention to the fact that use of soluble adjuvants that are readily dispersed from the injection site and has no depot effect such as saponin are routine in the art of vaccine preparation. Wu et al. teach that saponins from Q. saponaria have been identified as potent adjuvants and have been studied most

thoroughly in the form Quil A. This saponin mixture has been shown to augment antibody responses to both T-dependent and T-independent antigens and to induce antigen- specific helper T lymphocyte memory (see Wu et al. page 1524).

New Rejections

8. Newly added claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Green et al. (The veterinary record, May 2, 1987) and Geresi et al. (Ann. Immuno. Hung Vol. 25, pp. 37-40 1985) in view of Wu et al. (The Journal of Immunology, Vol. 148, pp. 1519-1525, 1992) and Gluck et al. (US Patent 5,879,685).

Claim 20 is drawn to a multicomponent clostridial vaccine composition comprising a viral antigen and a saponin adjuvant.

Note: The embodiments of newly added claim 20 is basically the same as previously rejected claim 18. For the rejection see paragraph 7 above.

Conclusion

9. No claim is allowed.

10. Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol Shahnan-Shah whose telephone number is (703) 308-8896. The examiner can normally be reached from 7:30 AM - 4 PM on Monday through Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned to is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Khatol Shahnan-Shah, BS, Pharm, MS

Biotechnology Patent Examiner

Art Unit 1645

August 21, 2004

RODNEY P SWARTZ, PH.D
PRIMARY EXAMINER